Sheets of human retinal progenitor transplants improve vision in rats with severe retinal degeneration.

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Funding Grants: Restoring vision by sheet transplants of retinal progenitors and retinal pigment epithelium (RPE) derived from human embryonic stem cells (hESCs)

Public Summary:
Loss of photoreceptors and other retinal cells is a common endpoint in retinal degenerate (RD) diseases that cause blindness. Retinal transplantation is a potential therapy to replace damaged retinal cells and improve vision. In this study, we examined the development of human fetal retinal sheets with or without their retinal pigment epithelium (RPE) transplanted to immunodeficient rats with severe RD. Sheets were dissected from immature human eyes (11-15.7 weeks gestation) and then transplanted to the subretinal space of 24-31 d old RD nude rats. Every month post surgery, eyes were imaged in vivo by high-resolution spectral-domain optical coherence tomography (SD-OCT). SD-OCT showed that transplants were placed into the subretinal space and developed laminated areas or rosettes, with clear development of plexiform layers first seen in OCT at 3 months post surgery. Several months later, as could be expected by the much slower development of human cells compared to rat cells, transplant photoreceptors developed inner and later outer segments. Retinal sections were analyzed by immunohistochemistry with antibodies for human and retinal markers. This confirmed the formation of several retinal subtypes within the retinal layers. Transplant cells extended processes and many cells could also be seen migrating into the host retina. At 5.8 – 8.6 months post surgery, selected rats were exposed to light flashes and recorded by electrophysiology for visual responses in a visual center in the midbrain (superior colliculus). Four of seven rats with transplants showed responses to flashes of light in a limited area. No response with the same dim light intensity was found in age-matched RD controls (non-surgery or sham surgery). In summary, our data showed that human fetal retinal sheets transplanted to the severely disturbed subretinal space of RD nude rats develop mature photoreceptors and other retinal cells, integrate with the host and induce vision improvement.

Scientific Abstract:
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